--48. The method of claim 47, wherein said bacteria is *Sporolactobacillus* P44.--

--49. A method of increasing the solubility and bioavailability of nutritional materials within the gastrointestinal tract of an animal or, preferably, a human, comprising the administration of a therapeutically-effective concentration of one or more non-pathogenic, lactic acid-producing bacteria within a pharmaceutically-acceptable carrier suitable for administration to the gastrointestinal tract of a vertebrate, wherein said lactic acid-producing bacteria increases the solubility and bioavailability of nutritional materials within the gastrointestinal tract of said vertebrate, wherein said bacteria is a *Bifidiobacterium*.--

--50. The method of claim 49, wherein said bacteria is selected from a group consisting of *Bifidiobacterium adolescentis*, *Bifidiobacterium animalis*, *Bifidiobacterium breve*, *Bifidiobacterium infantis*, *Bifidiobacterium infantis*, and *Bifidiobacterium longum*.--

REMARKS

Upon entry of these amendments, claims 1, 3-20, 22, and 25-50 will be pending.

As suggested by the Examiner, the claims were amended to better define the claimed invention. Specifically, reference to a "therapeutic composition" has been amended to recite -- composition-- and the term "therapeutically-effective concentration" has been deleted. These aforementioned amendments add no new matter. Claim 1 was amended to incorporate the limitations of claim 2; claim3, 4, and 5 were amended to put them into independent form. Claim 20 was amended to incorporate the limitations of claim 21, and claim 22 was put into independent form. New claims 45 and 46 are supported by originally-filed claims 4 and 5, and new claims 47-50 are supported by originally-filed claims 23 and 24.

Additionally, a claim for priority to U.S. Provisional Application Serial Number 60/095,786, filed August 6, 1999, has also been added.

III. Rejection of Claims Under 35 U.S.C. §102(b)

All of the pending claims were rejected for anticipation by Fuller or Friend et al. This rejection is traversed.

The controlling law for anticipation is set forth in *Scripps Clinic & Research Foundation v. Genentech. Inc.*, 927 F.2d 1565, 18 USPQ2d 1001 (Fed. Cir. 1991); *limited reconsideration* 18 USPQ2d 1896 (Fed. Cir. 1991) in which the court held that ***all*** the elements of the claim limitations must be found in a ***single*** prior art reference and that reference must be enabling, such that it teaches the public how to make and use the claimed subject matter. Both *Fuller* and *Friend* fail to meet this requirement for several reasons.

The Examiner has rejected claims 1-44 under 35 U.S.C. §102(b) as allegedly being anticipated by Fuller, History and Development of Probiotics, In: *Probiotics: The Scientific Basis,* Fuller, ed. pp. 1-8 Chapman & Hall (1992) (*"Fuller"*). Specifically, the Examiner alleges that Fuller discloses that benefit[s] from "probiotic supplementation are numerous and include improved utilization of food [that] may be achieved by increased efficiency of existing digestive processes or by promoting the digestion of previously indigestible substances." *See, Office Action,* page 5, number 13 through page 6, number 15.

Independent claims 6, 19, 25, 38, 39, and 42 all require specific bacterial strains, which are not described in Fuller. Claim 1 and 20 were amended to incorporate the limitations of dependent claims which recite specific bacterial strains, which are not described by Fuller. Thus, the amended claims are not anticipated by this reference, and this rejection must be withdrawn.

The Examiner has also rejected claim 1-44 under 35 U.S.C. §102(b) as allegedly being anticipated by Friend and Shahani, Nutritional and Therapeutic Aspects of Lactobacilli, 1984. *J. Appl. Nutrition*, **36**: 125-153 (*"Friend"*). Specifically, the Examiner alleges that *Friend* discloses that "Lactobacilli have been shown to constitute one of the major groups of intestinal and fecal organisms in animals and humans and recent scientific evidence attests their importance in human nutrition and health" and "a number of studies have established that fermentation by the lactobacilli improves the nutritional value of food products by increasing the quantity as well as the availability, digestibility and assimilability of nutrients." *See, Office Action,* page 6, numbers 16-17.

Applicants have amended the claims to delete recitation of L. bugaricus and L. casei to overcome the rejection. Friend et al. does not described the strains of Lactobacillus now recited by the amended claims. In view of this amendment, Applicants request withdrawal of this rejection.

Rejection of Claims Under 35 U.S.C. §112, First Paragraph

First Issue:

The Examiner has rejected claims 1-44 under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. *See,* Office Action, page 2, number2.

Specifically, the Examiner has alleged that claims 1-44 are drawn to "therapeutic compositions" or methods comprising a "therapeutically-effective concentration" of one or more non-pathogenic, lactic acid-producing bacterial species that possess the ability to increase the solubility and bioavailability of nutritional materials within the gastrointestinal tract. The Examiner has also alleged that while the Specification discloses a variety of bacterial strains and their concomitant function(s) and teaches formulations of vitamins/minerals to be used for delivery in combination with said bacterial strain(s), it fails to teach what therapy the "therapeutic compositions" and the methods comprising "therapeutically-effective concentrations" would be treating, thus it is unclear as to what is the therapy that these compositions are addressing.

As previously stated, and as suggested by the Examiner, claims 1-25 and 28-42 have been amended so as to better define the claimed invention, wherein reference to a "therapeutic composition" has be amended to recite --composition-- and the term "therapeutically-effective concentration" has been deleted.

Second Issue:

The Examiner has also alleged that the delivery of bacteria and probiotic organisms in general is considered unpredictable. Specifically, the Examiner has alleged that Ziemer, *et al.,* (1998. *Int. Dairy J.* **8**: 473-479) ("*Ziemer*") teaches that for effective oral delivery of probiotic microorganisms, the bacteria must first survive the conditions of the stomach and small intestine before reaching colon of the large intestine, where a probiotic effect can potentially be seen. Additionally, *Ziemer* allegedly demonstrates that a major problem using probiotic strains of bacteria is "the inability of the fed organism to colonise the colon and become part of the microbial community." Therefore, the Examiner has alleged that it would require undue

experimentation for one skilled in the art to determine whether or not a specific strain of non-pathogenic, lactic acid-producing bacteria could be successfully delivered, *in vivo*. *See, Office Action,* pages 3-4, number 7.

Applicant respectfully disagrees with the Examiner's rejection and traverses. *Ziemer* only discusses the use of probiotic, lactic acid-producing *Lactobacilli* and *Bifidobacteria* bacterial species. Claims 3 and 5, reciting compositions using *Lactobacilli* and *Bifidobacteria,* have been cancelled. In contrast, the present invention expressly clearly discloses and claims compositions using *Bacillus coagulans* (*see,* Claim 6). With respect to *Bacillus coagulans,* the Specification states that: "*Bacillus coagulans* is able to survive and colonize the gastrointestinal tract in the bile environment and even grown in this low pH range"; whereas other "classic *Lactobacillus* species are unsuitable for colonization of the gut due to their instability in the harsh (*i.e.,* acidic) pH environment of the bile, particularly human bile". *See, Specification,* page 14, lines 13-17. The Specification also discloses that the human bile environment is different from that of animal models, and prior to the present invention, there have not been any accurate disclosure of *Bacillus coagulans* growth in the human gastrointestinal tract. *See, Specification,* page 14, lines 17-20.

Moreover, *Bacillus coagulans* possesses the following unique physiological characteristics (*see, e.g.,* Bergy's Manual (Seventh Edition)) which differentiate it from other lactic acid-producing bacterial species, and lend support to its' ability to survive the inhospitable environment of the gastrointestinal tract. These characteristics include, but not limited to:

(*i*) *Bacillus coagulans* is a Facultative Aerobe and possesses the to grow well in either environments that have free-oxygen or in strictly anaerobic environments. This is important due to the fact that *Lactobacilli* and *Bifidobacteria* are not aero-tolerant and thus proliferate in environments containing free-oxygen.

(*ii*) *Bacillus coagulans* is highly Thermo-Tolerant. The vegetative cells of *Bacillus coagulans* possess the ability to grow at temperatures as high as 65°C, whereas the endospores can withstand temperatures in excess of 100°C. In fact, *Bacillus coagulans*, along with *Bacillus stereothermophilus*, is used for quality control purposes in autoclaves. The thermo-tolerant nature of *Bacillus coagulans* is in direct contrast to that of **all** species of *Lactobacilli* and *Bifidobacteria*, which typically cannot grow in temperatures greater than 45°C and cannot survive temperatures greater than 65°C.

(*iii*) *Bacillus coagulans* is Halo-Tolerant and possesses the ability to grow in highly alkaline environments including 7% NaCl or 10% caustic soda.

(*iv*) *Bacillus coagulans* is Acid-Tolerant and possesses the ability to grow in highly acidic environments including *e.g.*, pH 2.0 HCl.

Third and Fourth Issues:

With respect to the third issue, the Examiner has further alleged that the Specification does not teach that the disclosed formulation(s) will provide a therapeutic effect, *in vivo*. Hence, it is unclear that the administration of the therapeutic composition of bacteria and vitamins and/or minerals will increase the solubility and bioavailability of nutritional materials within the gastrointestinal tract. For example, the Examiner has alleged that Salminen, *et al.*, (1998. *British J. Nutrition* **80(Suppl. 1)**: S147-S171) ("*Salminen*") teaches that "the colonic microflora is a complex interactive community of organisms and its functions are a consequence of the combined activities of the microbial components" and thus, "[d]isturbances of the intestinal microflora may lead to other disturbances and dysfunctions of the gut...and may disturb the microflora in a manner such as to not see an effect by the delivered composition". *See, Office Action,* page 4, number 8.

Additionally, the Examiner has alleged that the Specification gives no guidance as to what therapeutic strains are suitable for which organisms and no examples of any success seen upon delivery of said therapeutic composition, as the fate of the delivered vitamins/minerals in terms of solubility and availability would rely, at least in part, on the bacterial strain(s) utilized in the therapeutic composition, as well as the preexisting microflora of the animal accepting the therapeutic composition. Therefore, the Examiner has alleged that it would require undue experimentation to determine, the strain(s) of bacteria needed for each species of animal and for each composition of vitamins/minerals to elicit a therapeutic effect. *See, Office Action,* pages 4-5, number 9.

With respect to the fourth issue, the Examiner has alleged that the Specification provides no guidance to one skilled in the art in the selection of which bacteria for: (1) therapeutic treatment of which ailment and (2) increasing the solubility and bioavailability of which nutrient(s). While the Examiner has conceded that the Specification discloses a variety of species and strains of bacteria and varying therapeutic compositions (including multiple vitamins and minerals), he has alleged that it fails to teach which therapeutic compositions of which species of bacteria and in which formulation with certain vitamins and minerals should be used

for the treatment of which ailment(s). Thus, the Examiner has alleged that it would require undue experimentation for one skilled in the art to determine which therapeutic composition is to be used for which specific ailment. *See, Office Action,* page5, number 10.

Applicant traverses with respect to both the third and fourth issues set forth above for the following reasons. First, Applicant respectfully submits that the Examiner's lack of enablement rejection under 35 U.S.C. §112, first paragraph is, in effect, a lack of utility rejection which has been veiled as a lack of enablement rejection. The requirement of 35 U.S.C. §112, first paragraph as "to how to use" the invention is different from the utility requirement of 35 U.S.C. §101 (*see,* MPEP §2164.07) which requires that some use be set forth for the invention, and that the use be provable and not against public policy.

Applicants further respectfully submit that this rejection under 35 U.S.C. §112, first paragraph, is clearly contrary to the principles set forth in the UNITED STATES PATENT AND TRADEMARK OFFICE Utility Examination Guidelines. *See,* 60 *Fed. Reg.* 36263-36265, (July 14, 1995). These Guidelines and the accompanying legal analysis ("Legal Analysis"), are relevant to rejections based upon lack of utility, whether cited under 35 USC §101, or for "failure to teach how to use" under 35 U.S.C. §112, first paragraph, as in the present case.

The present invention provides ample disclosure on how to use the invention. For example, the Specification discloses: (*i*) numerous strains of probiotic bacteria (including *Bacillus coagulans*) and their culture conditions on, *e.g.,* page 9, line 22 through page 17,line 13; and (*ii*) therapeutic composition, including specific formulations on, *e.g.,* page 19, line 11 through page 26, line 38. Accordingly, the Applicant respectfully reminds the Examiner that "[a]s long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the scope of the claim, then the enablement requirement of Section 112 is satisfied." *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

It is well-settled that, "[c]ompliance with the enablement requirement of 35 U.S.C. §112, first paragraph does not turn on whether an example is disclosed." MPEP §2164.02. There is no statutory requirement for the disclosure of a specific example, "...[a] patent Specification is not intended, nor required to be a production specification." *In re Gay,* 309 F.2d 768, 771, 135 USPQ 311, 314 (CCPA 1962). Moreover, "[a]n example may be 'working' or 'prophetic,' and

an applicant need not have actually reduced the invention to practice prior to filing." *Gould v. Quigg,* 822 F.2d 1074, 1078, 3 USPQ 2d 1302, 1304 (Fed. Cir. 1987); MPEP §2164.02.

Second, with respect to any requirement for human testing, the MPEP expressly states that human clinical data is *not* required for enablement under 35 U.S.C §112, first paragraph. With respect to this issue, the MPEP expressly states:

> **Office personnel should not impose on applicants the unnecessary burden of providing evidence from human clinical trials.** There is no decisional law that requires an applicant to provide data from human clinical trials to establish utility for an invention related to treatment of human disorders (*see, In re Isaacs*, 347 F.2d 889, 146 USPQ 193 (CCPA 1963); *In re Langer*, 503 F.2d 1380, 183 USPQ 288 (CCPA 1974)), even with respect to situations where no art-recognized animal models existed for the human disease encompassed by the claims.

MPEP §2107.02.IV [emphasis added].

The MPEP further states that:

> **The applicant does not have to prove that a correlation exists between a particular activity and an asserted therapeutic use of a compound as a matter of statistical certainty, nor does he or she have to provide actual evidence of success in treating humans where such a utility is asserted.** Instead, as the courts have repeatedly held, all that is required is a reasonable correlation between the activity and the asserted use. *Nelson v. Bowler*, 626 F.2d 853, 857, 206 USPQ 881, 884 (CCPA 1980).

MPEP §2107.02.I [emphasis added.].

On the basis of the foregoing arguments, Applicant respectfully requests that the Examiner reconsider and withdraw the rejection of claims 1-44 under 35 U.S.C. §112, first paragraph.

CONCLUSION

On the basis of the foregoing amendments and remarks, Applicant respectfully submits that the pending claims are in condition for allowance. If there are any questions regarding these amendments and remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,

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